Enabling Nano-Bio Science through Nanofabrication

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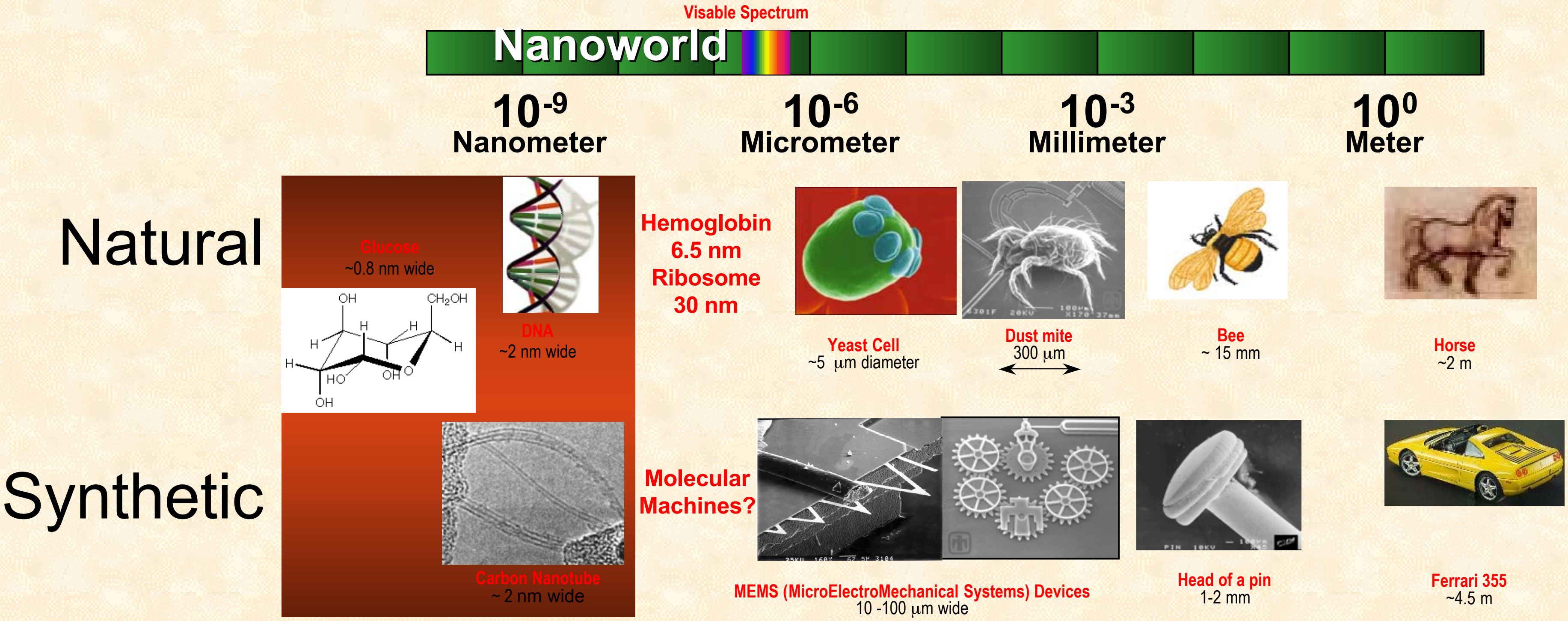
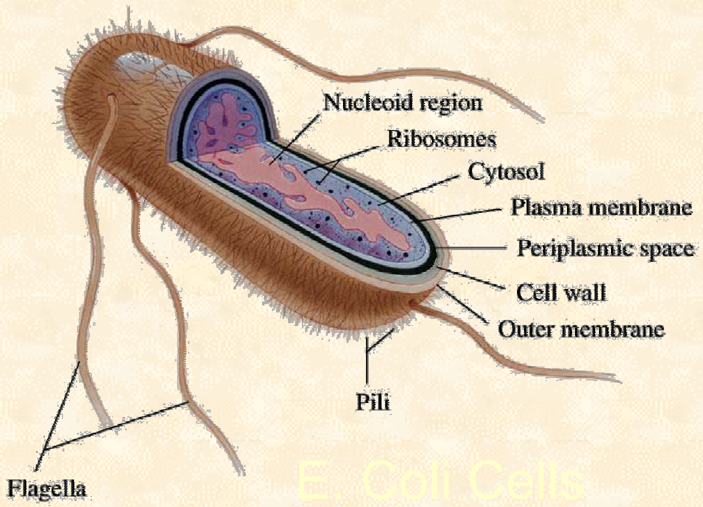
Overlap between biological and synthetic nanotechnology

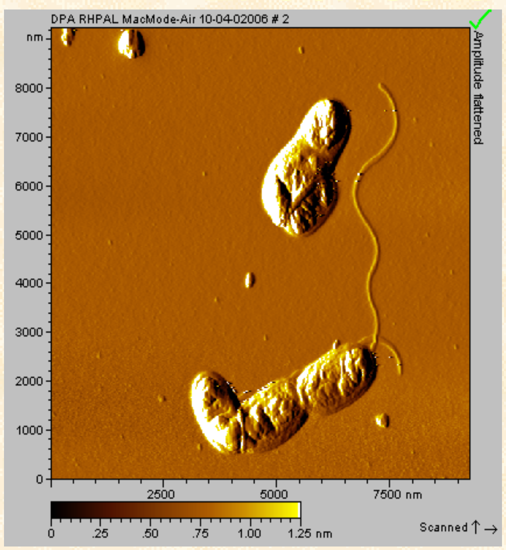


- Natural and synthetic devices merge at the nanoscale
- Opportunity to interface with biology
- Opportunity to exploit biological design principles

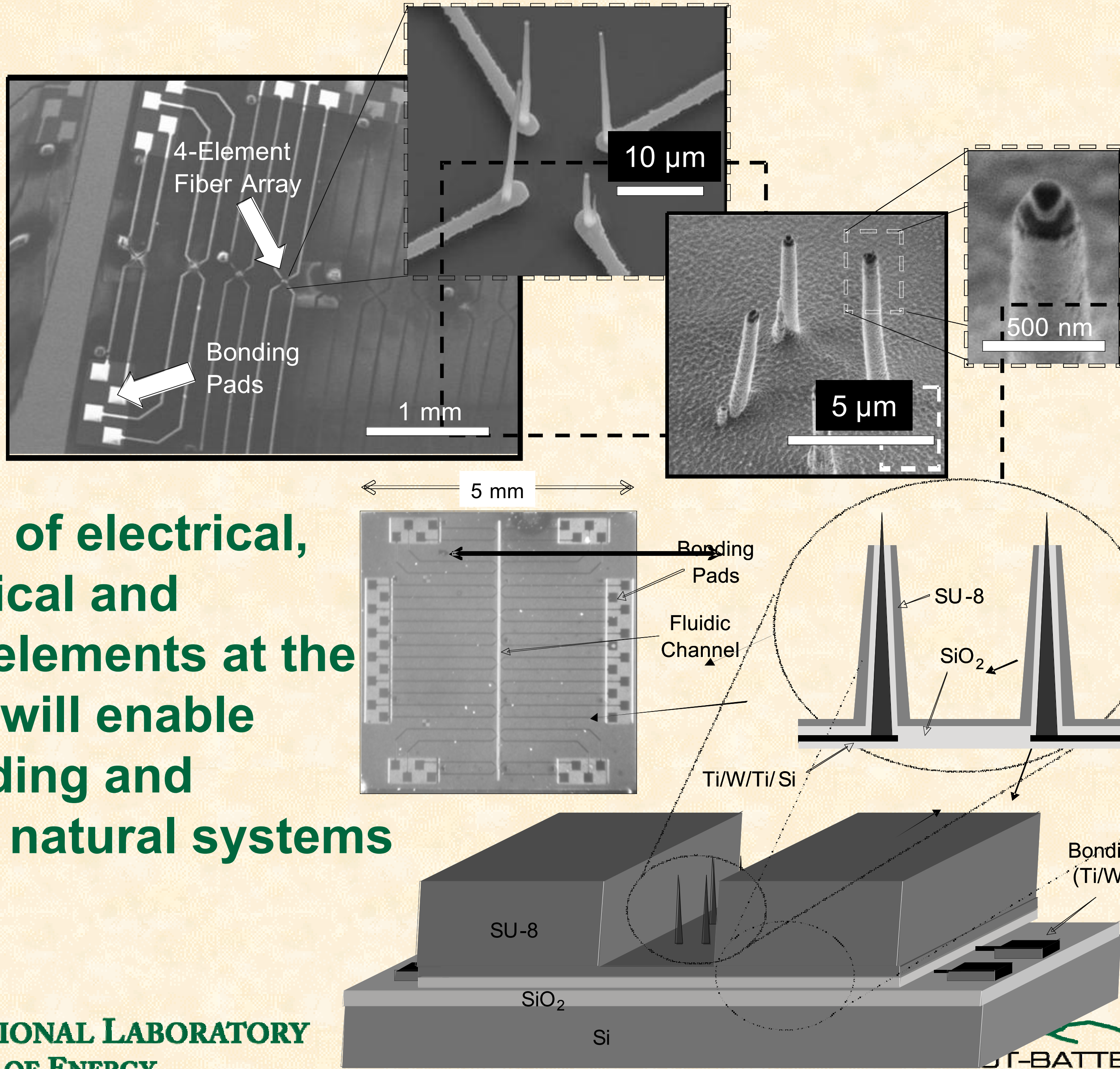
Complex NanoSystems: Cells



E. Coli Cells



- **Cells are the fundamental unit of biology**
  - **Control the flow of information, energy, and materials**
- **Dimensions and spatial arrangements are critical for function**
  - **Cell dimensions, ~2 microns**
  - **Cell volume, ~30 femtoliters**
  - **Membrane thickness, ~5 nm**
- **Biological Challenge: Understanding how multiple length scale features enable function**
- **Fabrication challenge: Creating multiple length scale structures**



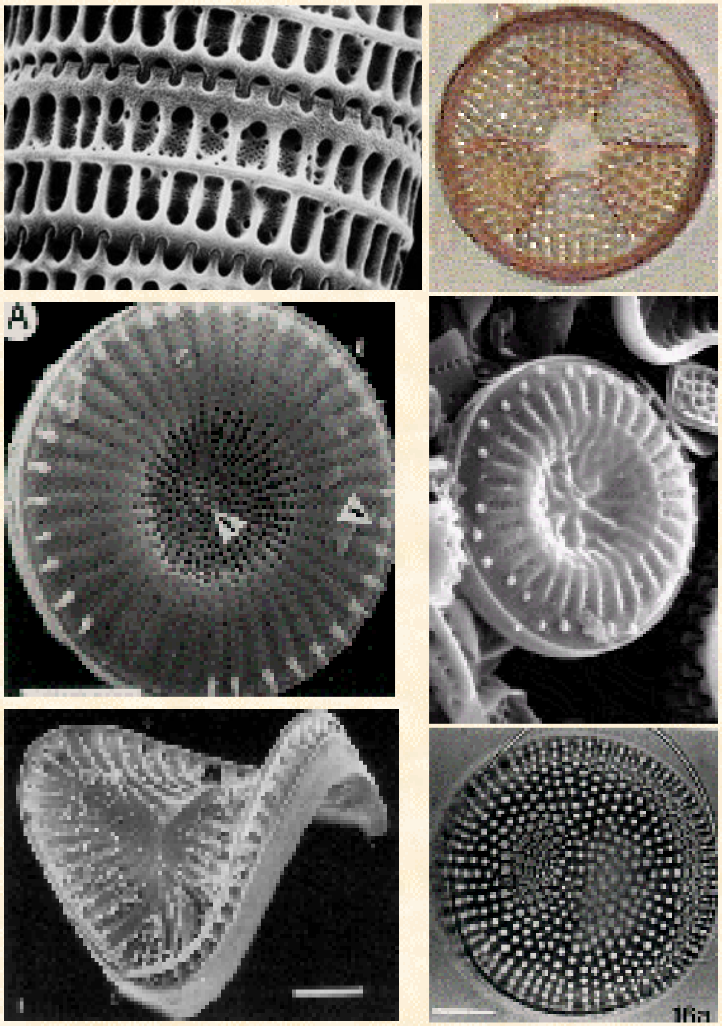
Integration of electrical, fluid, physical and biological elements at the nanoscale will enable understanding and mimicry of natural systems

Nanofabrication Research Laboratory

- Mike Simpson - Thrust Leader
- ORNL "Jump Start" fab facility
  - ~2300 total sq. ft. including 1100 sq. ft. of class 100 and 1000 clean room space
  - Limited (i.e. 'expert user') operation now
- Collaboration with the NanoProBE Center (proposed NNIN node) on University of Tennessee campus
  - Jump Start access to JEOL JBX-6000 E-beam stepper
  - Cooperative/complementary development of capabilities
  - User options

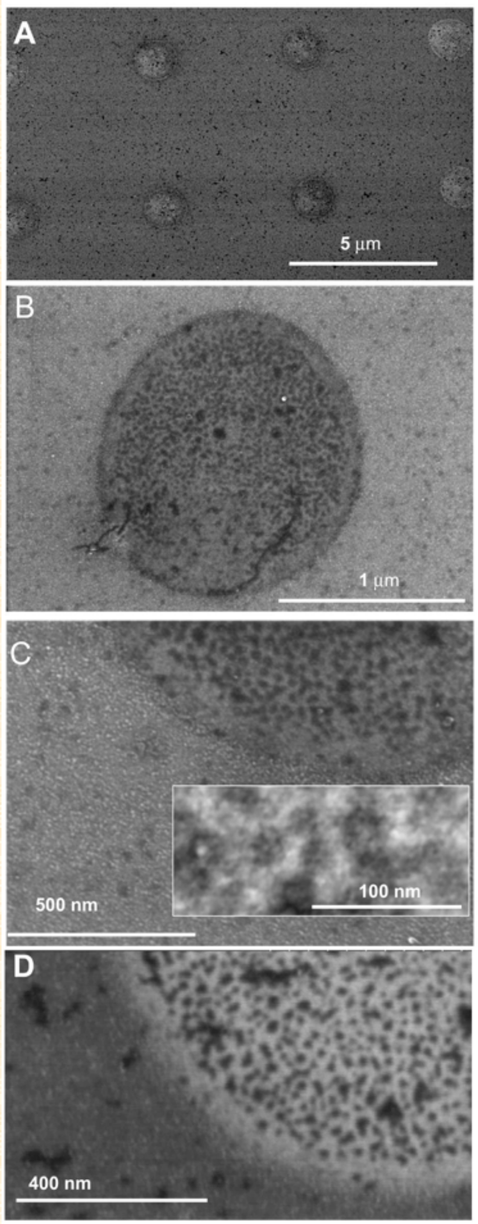
Directed assembly of inorganic materials by biomimetics

- Various marine organisms (diatoms, sponges, shellfish) facilitate silica synthesis
- Intricately designed shapes prepared under relatively mild conditions of temperature, pressure, pH
- Ultimately, genetic based instructions in combination with the environment are responsible for templating and catalyzing inorganic synthesis
- Controlled synthesis and directed assembly across multiple length scales!
- How does this happen? How is material transported and assembled across interfaces? Can similar principles be adapted for technological purposes?



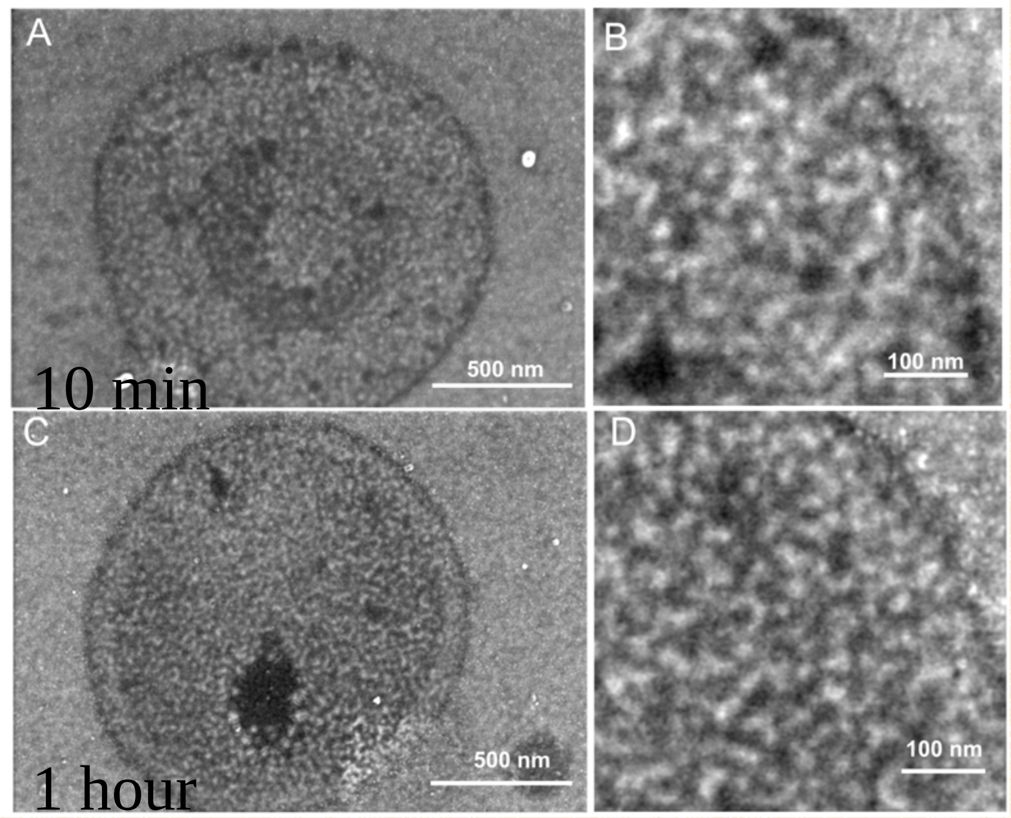
Silica synthesis from patterned PLL templates

- The molecular mechanisms of silica synthesis are being uncovered
  - Silicateins (Morse), siliffins (Kroger), lysine polymers (Mizutani)
  - The biopolymer templates and catalyzes silica formation
- Combining lithographic patterning technologies with biologically inspired catalysts to understand the molecular basis for directed assembly
- Yields thin laminate structures of interconnected silica particles where the PLL is patterned



Silica synthesis from patterned aminosilane reagent

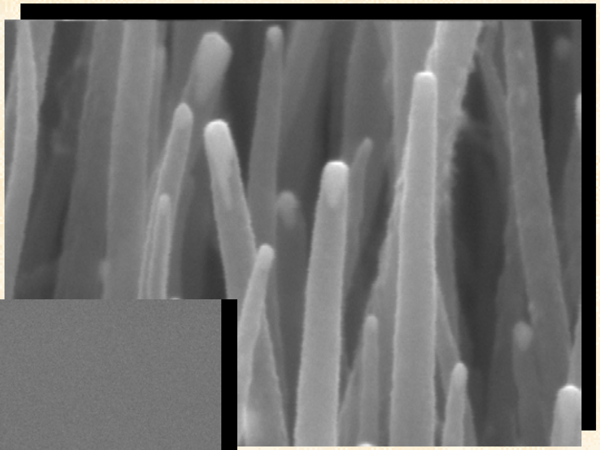
- Low molecular weight reagents precipitate silica in solution very slowly
- Propyl amine group mimics the function of the lysine residue
- Co-localization of functional groups effect templating and condensation of silicic acid
- Connecting the molecular to the microscopic!

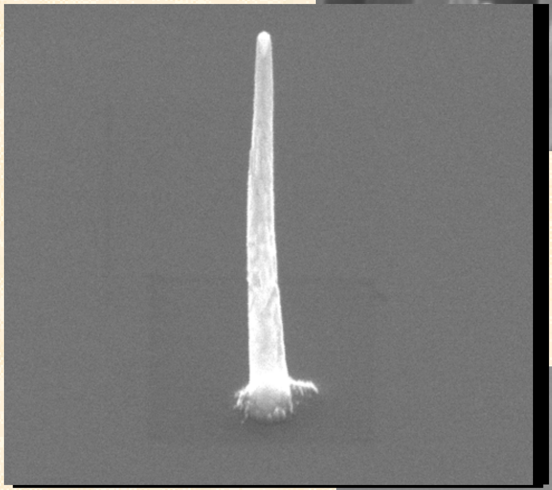


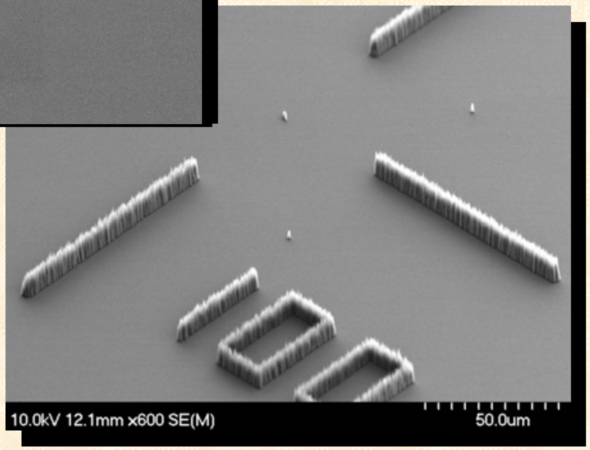
Coffman, Melechko, Allison, Simpson and Doktycz (2004) Langmuir, (in press)

Controlled CNF synthesis

- Grown by PE-CVD
  - Catalyst can be lithographically defined
- Deterministic Process
  - Position of CNFs can be controlled by placement of catalyst dots
  - Diameter controlled by catalyst dot size
  - Length controlled by growth time
- **Engineering on Multiple Length Scales!**



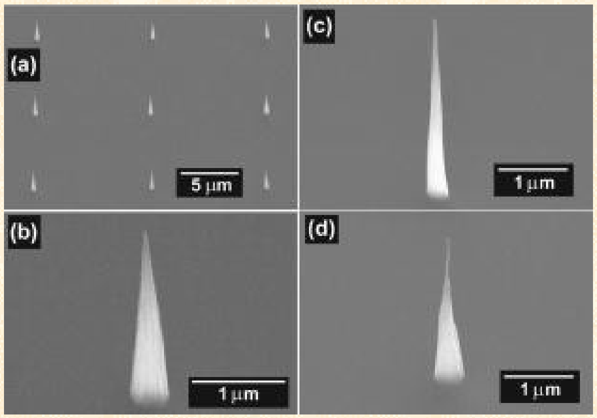




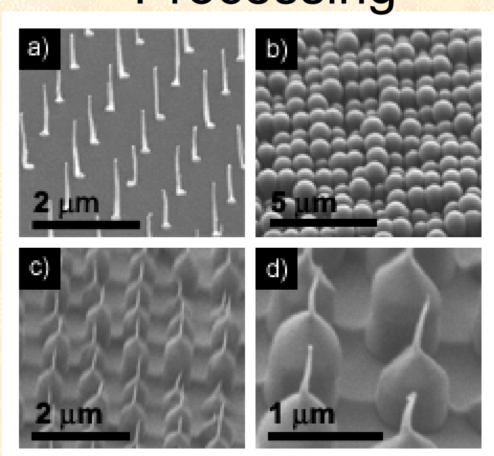
(Simpson and Lowndes, ORNL)

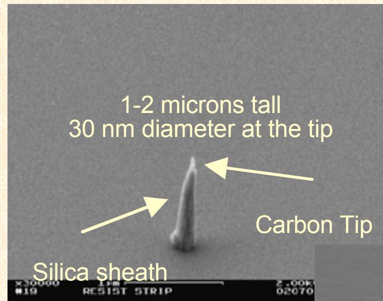
Nanofabrication

Shaping

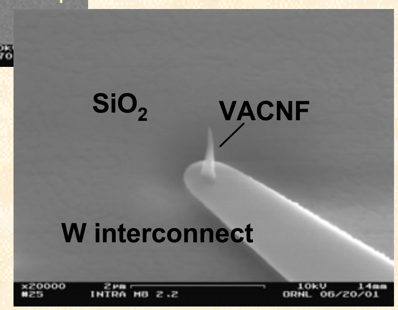


Processing

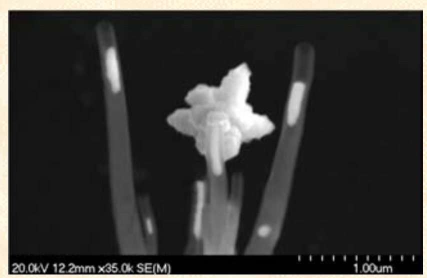




Addressing

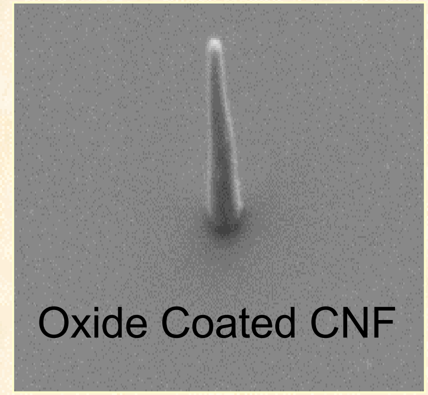


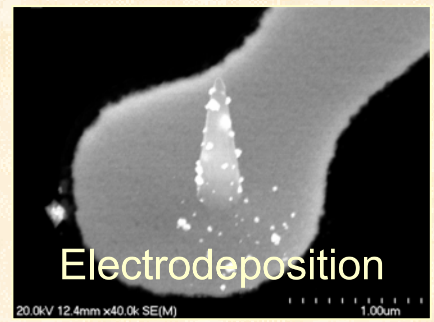
Nanopipe

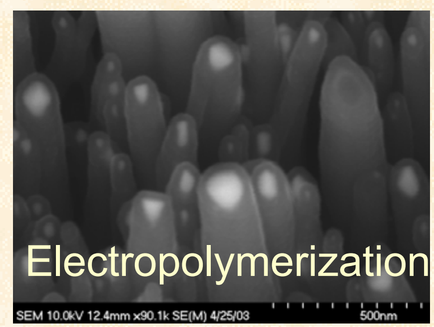


Templating

Chemical Coating

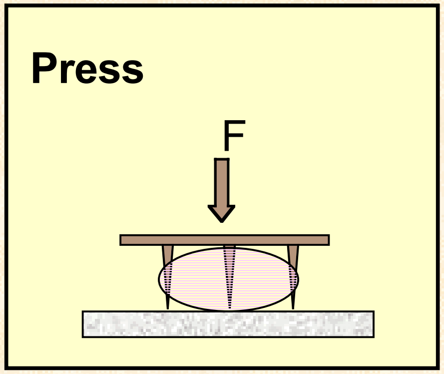


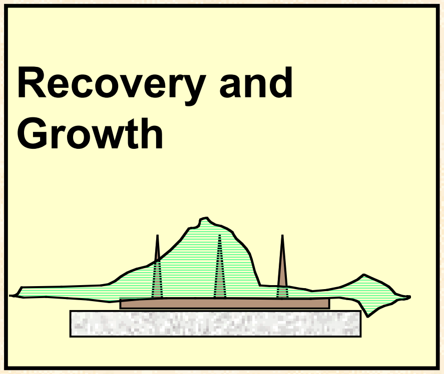


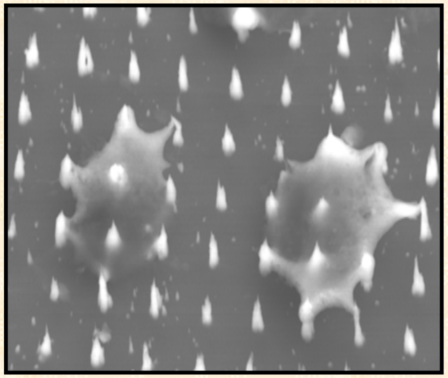


Cellular Interfacing

- Insertion of a nanoscale probe into live cells
- Gene/Protein delivery, intracellular sensing, intracellular sampling
- Information and material exchange with biological systems!

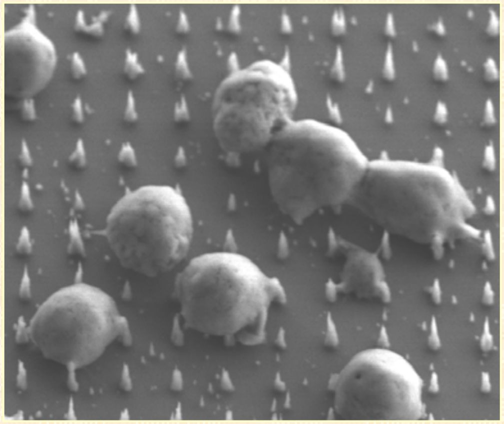


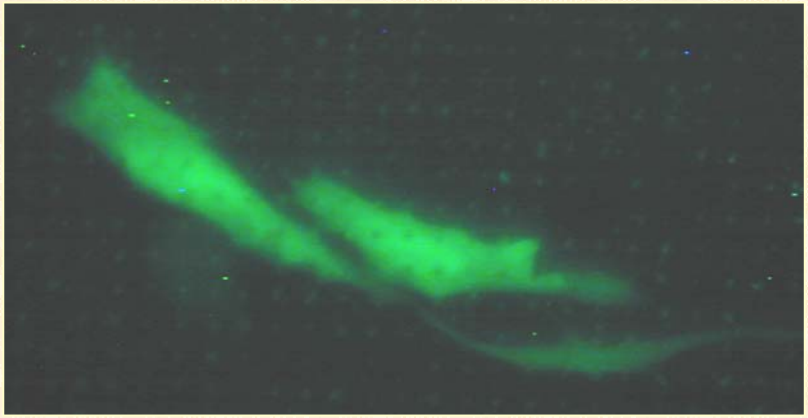




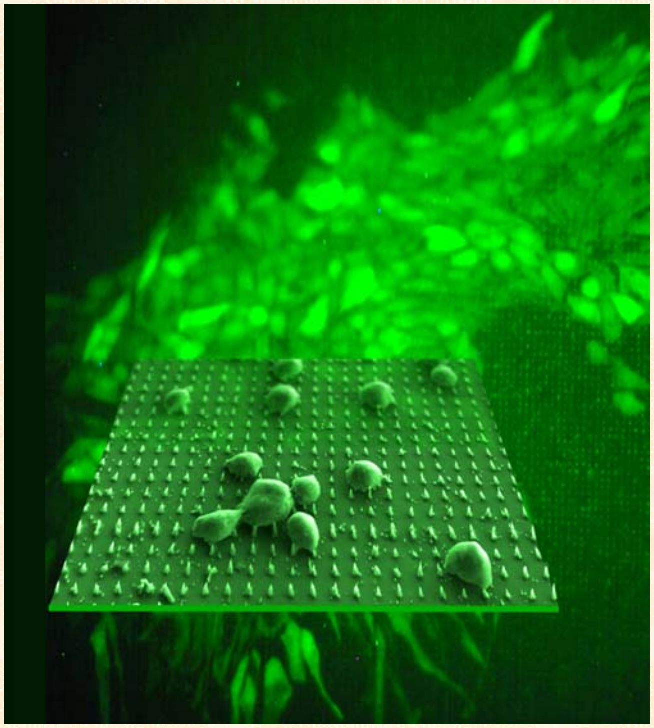
T. E. McKnight

GFP expression from DNA modified nanofibers provides an indicator of cellular penetration





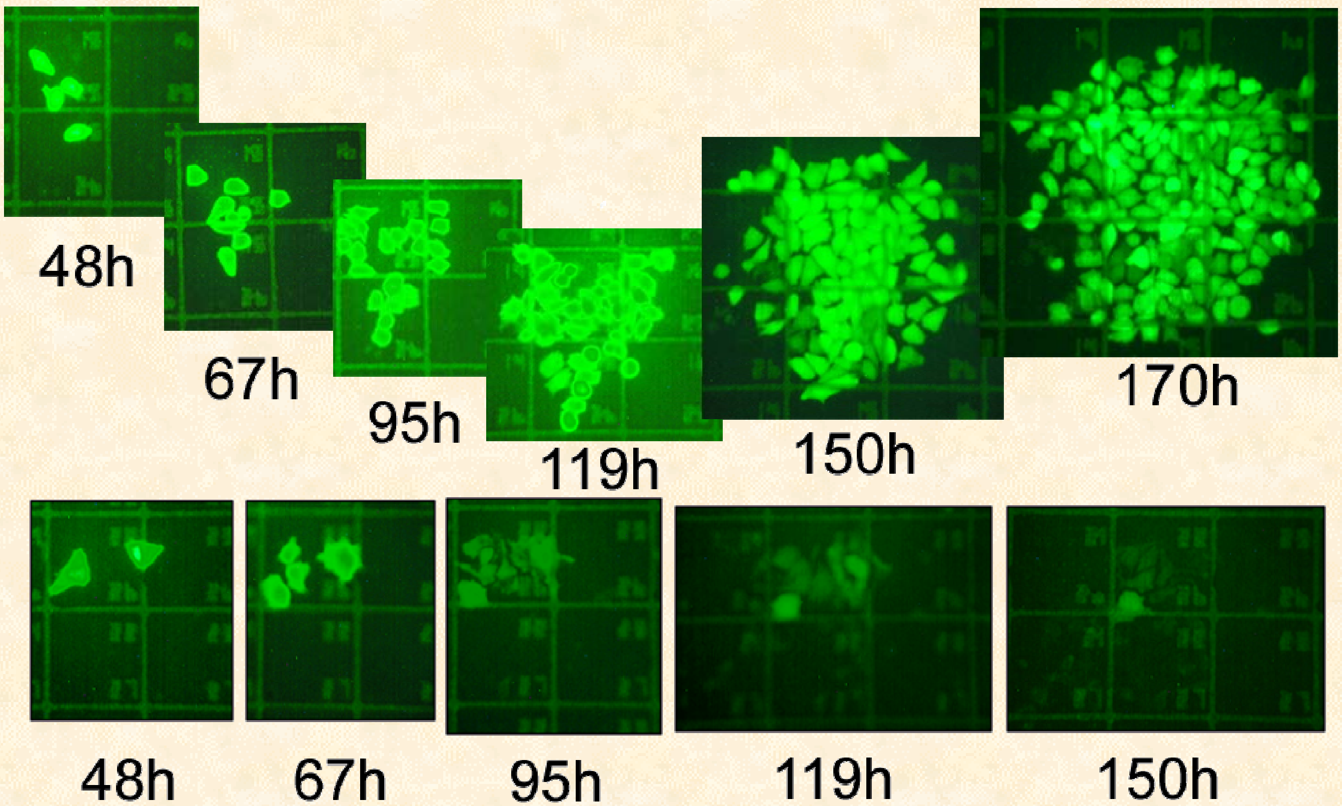
GFP expression from delivered plasmid 2 days following experiment



Fiber mediated plasmid delivery and expression of GFP in CHO cells 2 weeks following experiment

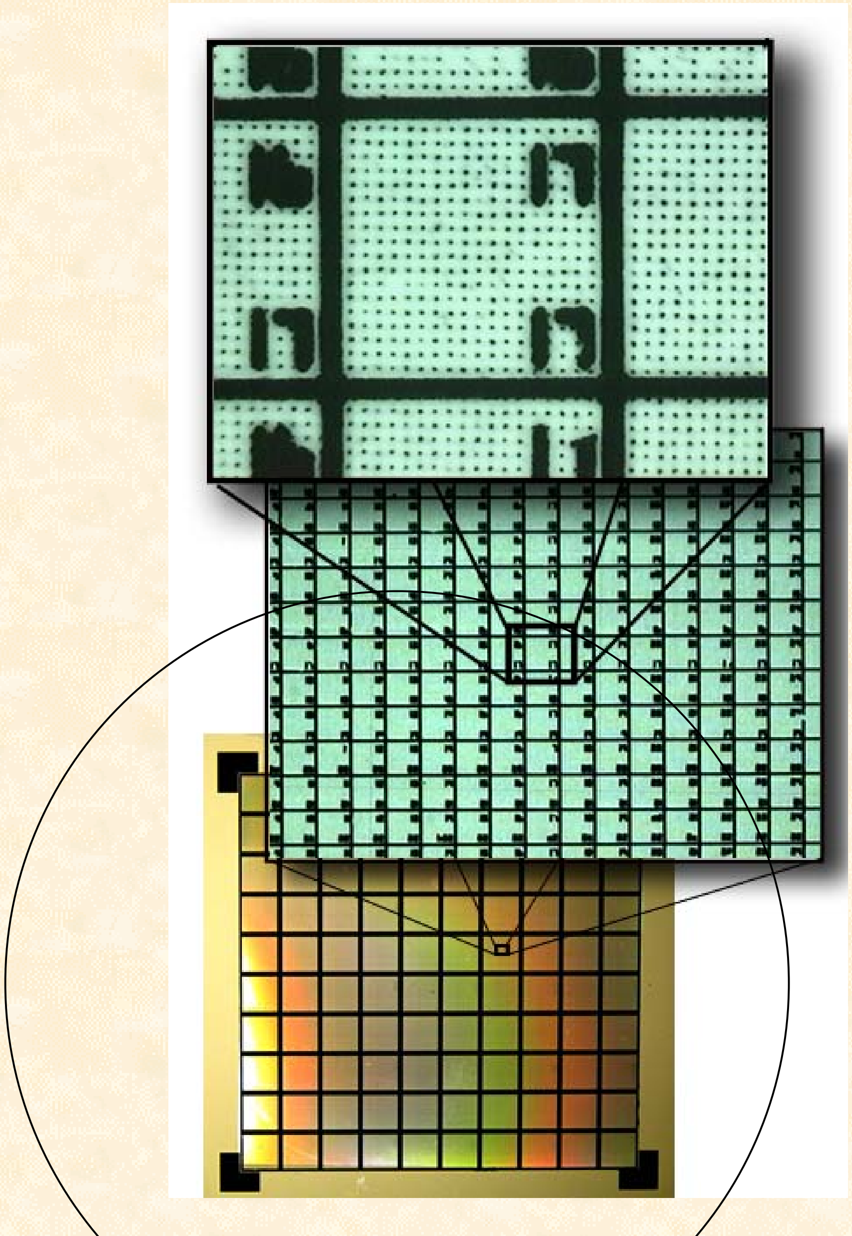
McKnight et al, Nanotechnology 14 (5), 551-556, 2003

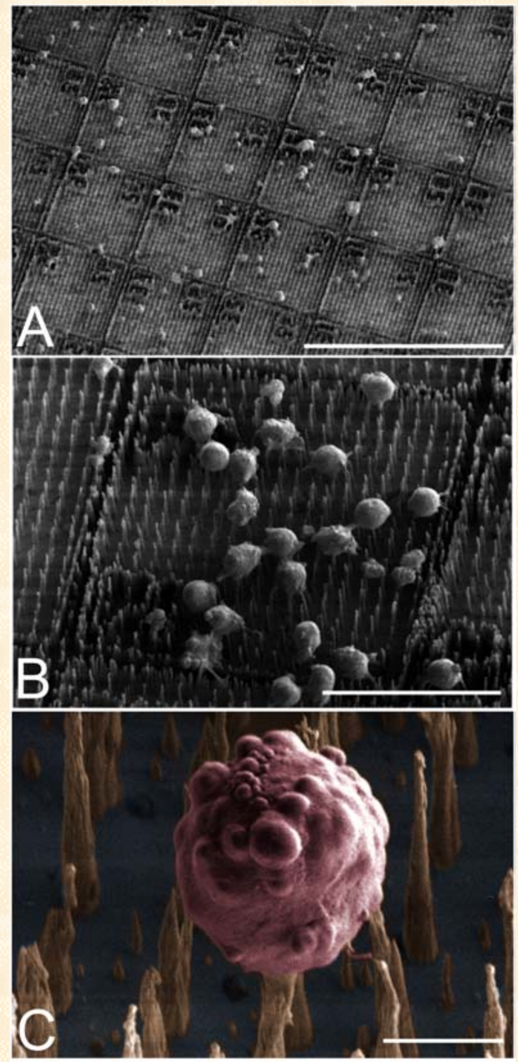
Expression of tethered genes from nanofiber scaffolding



T. E. McKnight

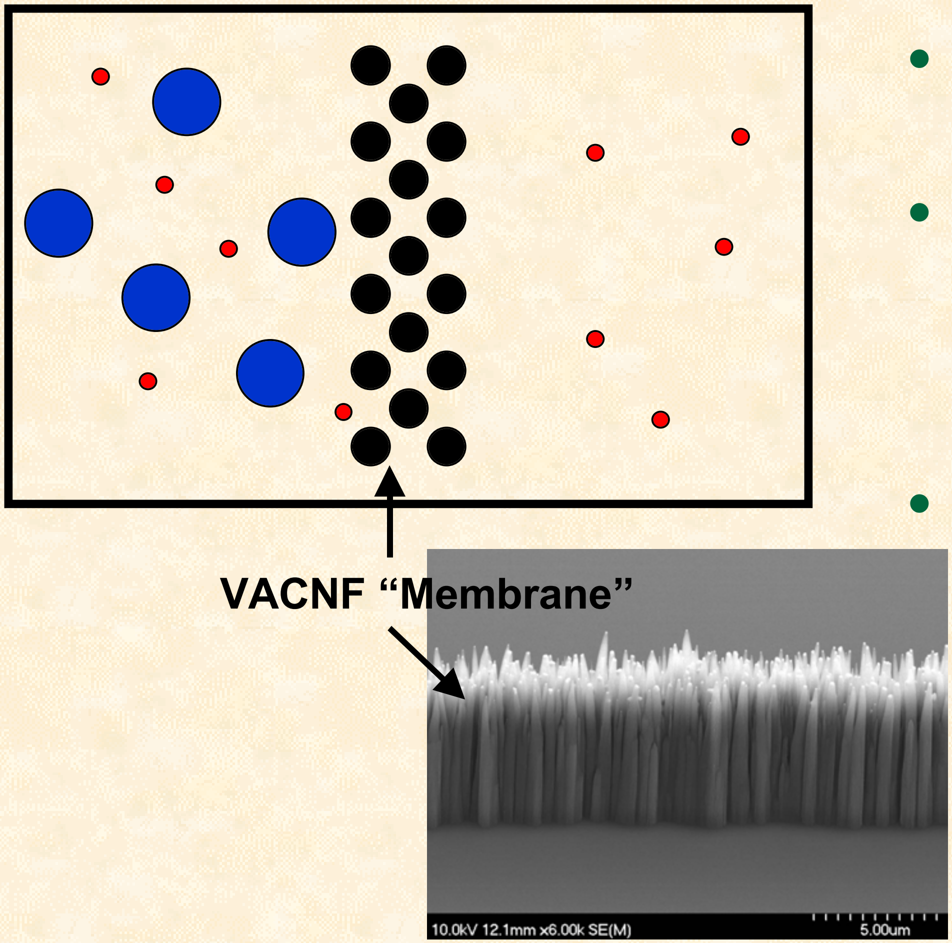
Wafer scale fabrication of gene delivery arrays.





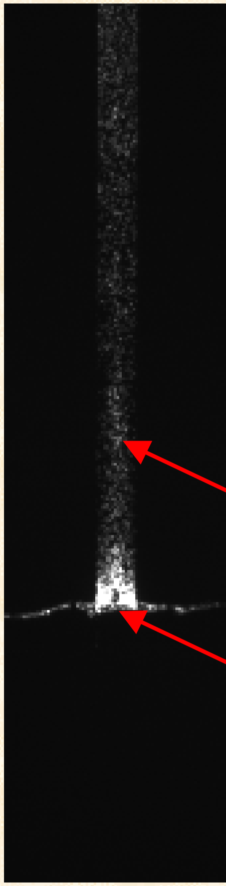
McKnight et al, NanoLetters, in press, 2004

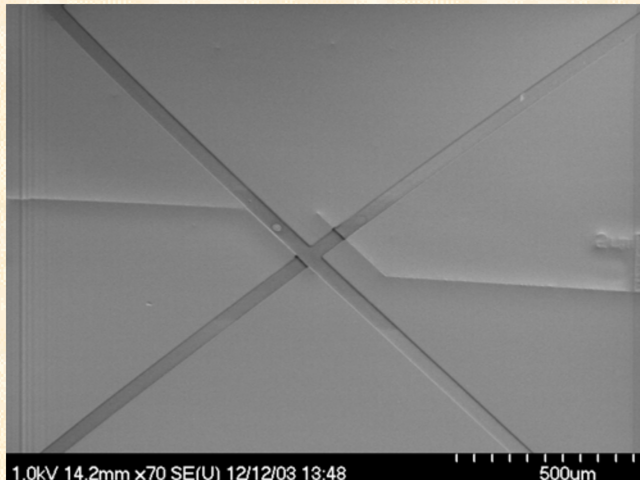
Arrayed Nanofibers as Transport Barriers



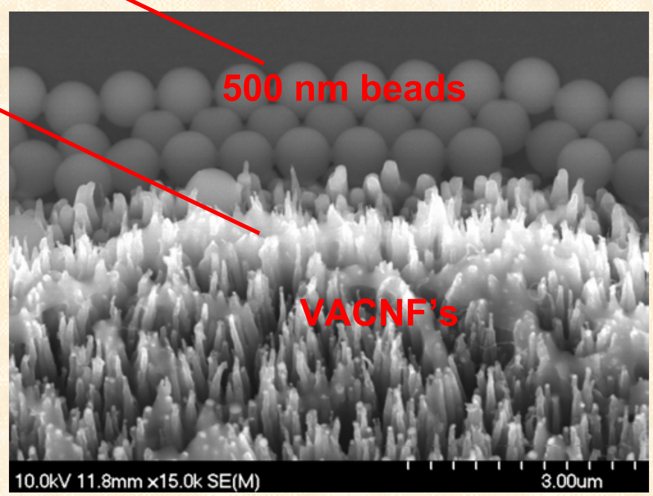
- Mimicking membranes
- Interfiber spacing acts as a molecular sieve
- Selective molecular transport based on physical/chemical properties of fibers
- Fabrication Challenge: Incorporating nanostructures with microfluidics for testing

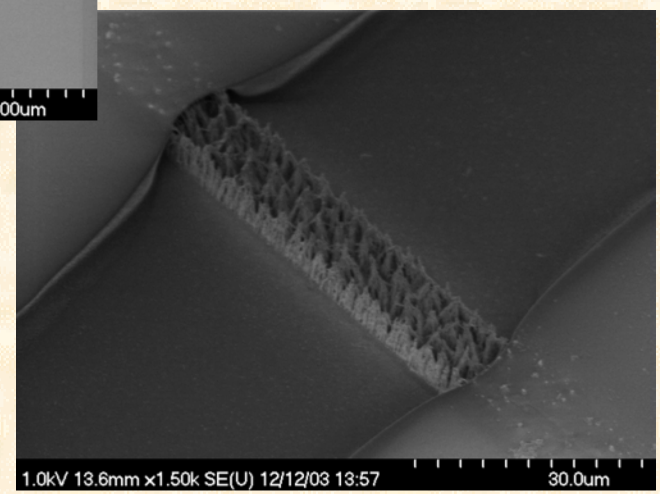
Restricted transport by VACNF barriers





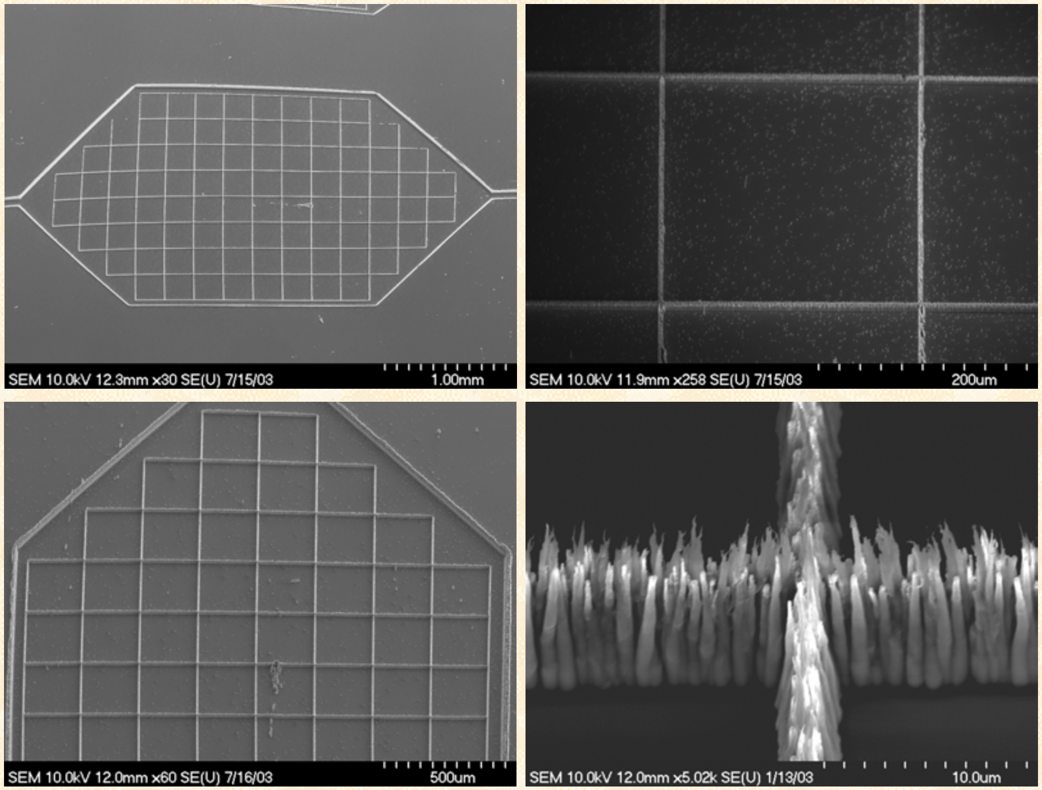
Integrating fluidic structures with nanofiber membranes





(Zhang et al, *Appl. Phys Lett*, (2002) 81(1), 135)

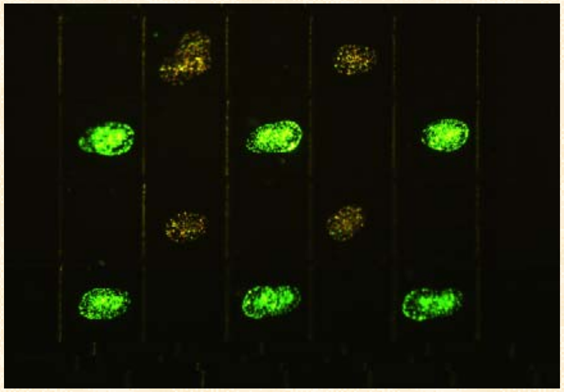
Cell Mimic Structures



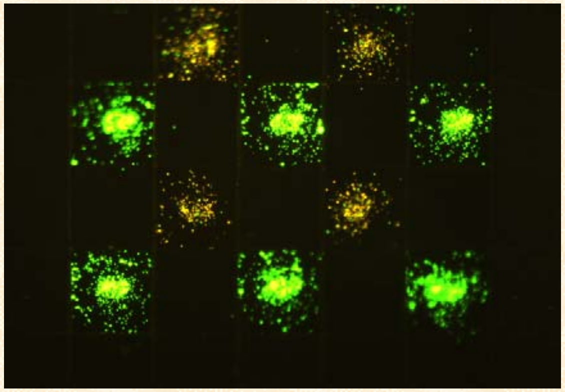
- Create appropriate physical environment for testing re-created biochemical networks
- Screening systems
- Integrate functions with molecular communication leading to multi-cellular tissue mimics for biomedical devices
- Need to fill and seal

Mimicking Cells

Different colored beads

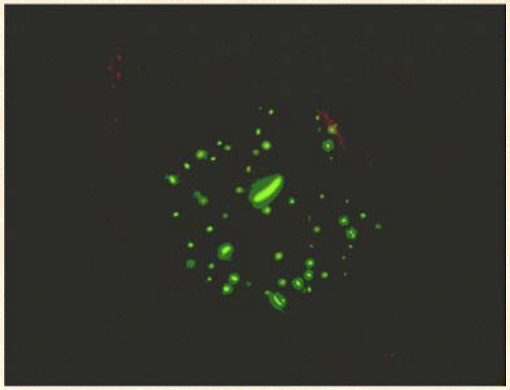


~15 pl dispense of latex beads

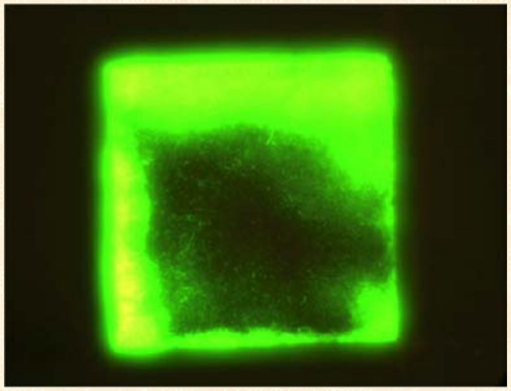


Sealed and filled cellular array (each cell volume ~250 pl)

GFP-labeled *E. coli*

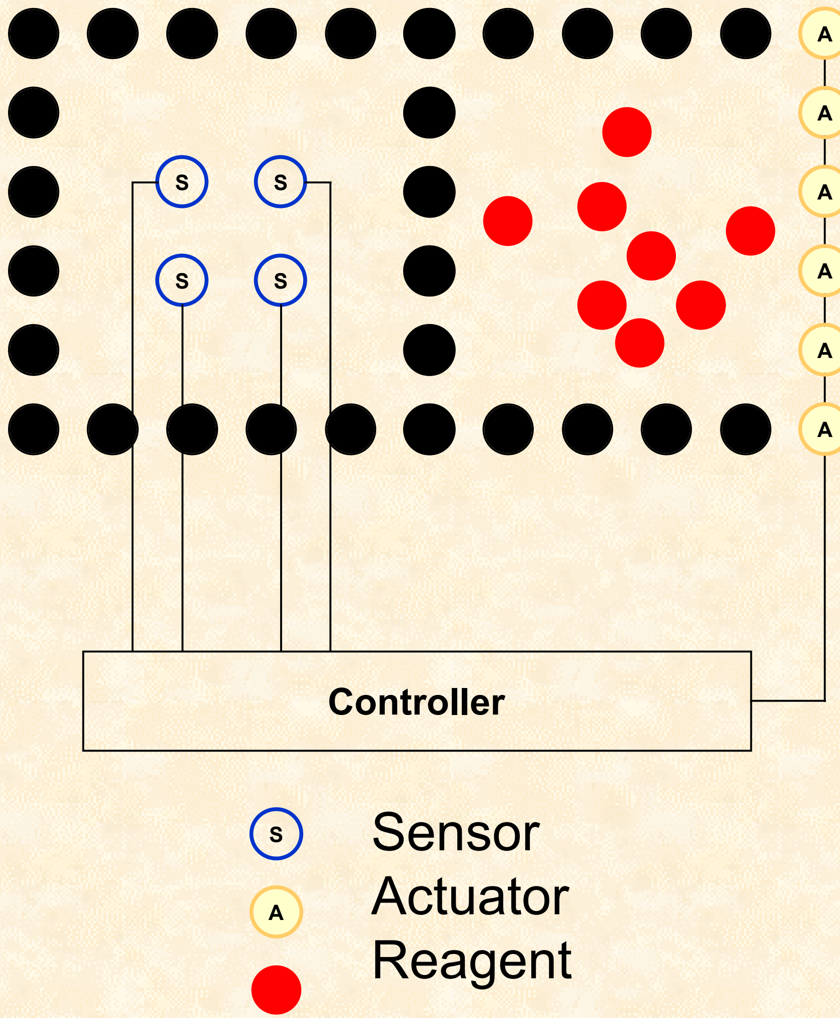


IJ dispense of microbes

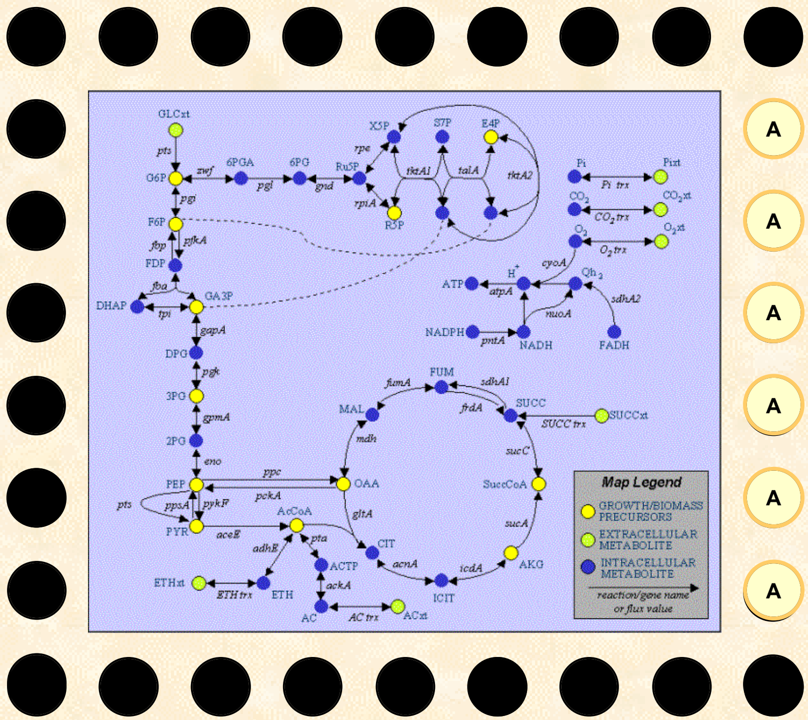


After overnight growth of microbes

Mimicking Cells



Mimicking Cells



Summary

- Significant overlap between biological and synthetic nanoscience - Controlling synthesis and directing assembly over multiple length scales
- Nanofabrication is key to enabling this science
  - Understanding how material synthesis occurs at interfaces
  - Transducing information and materials to living systems
  - Reconstructing and modeling complex reaction systems in physical environments that closely mimic natural conditions
  - Testing how spatial localization is used to control chemical reactivity and biological function
  - Studying of chemical signaling by chemotactic bacteria
- Capabilities are attracting a broad community of users